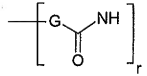
REMARKS

Favorable reconsideration of this application in view of the remarks to follow and allowance of the claims of the present application are respectfully requested.

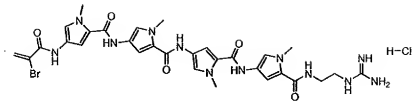
In the Official Action, Claims 1, 3, 5, 6, 9, 11, 13, 14, 24, 26 and 28-34 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. In addition, claims 1, 3, 5, 9, 11, 13, 14, 24, 26 and 28-34 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Finally, claims 1-3, 5-9, 11, 13-15 and 24-30 are rejected are rejected under 35 U.S.C. §103(a) as defining subject matter which is allegedly obvious over Cozzi et al.(WO 98/04525) in view of Cortes et al. *Investigational New Drugs* 18: 57-82, 2000 ("Cortes").

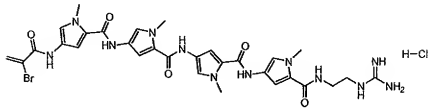
Before addressing the merits, it is noted that applicants have amended the claims. Specifically, claim 1 has been amended to define m as 0 or 1, n as 3 or 4, and r as 0, which definitions are within the scope of the original Markush group. It is to be noted that when r is 0,

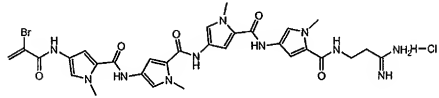


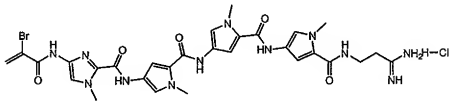
is a bond. In addition, applicants have limited the protein kinase inhibitor to ST-1571 and OSI-774 which is within the original Markush group.

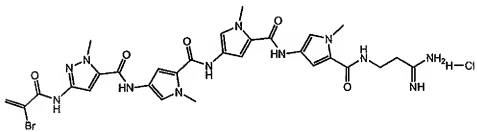
Applicants have amended the claimed subject matter to be closer in structure to that which is exemplified. More specifically, for the convenience of the USPTO, we have drawn the structure of the ten compounds listed on pages 6 and 7 of the instant specification.

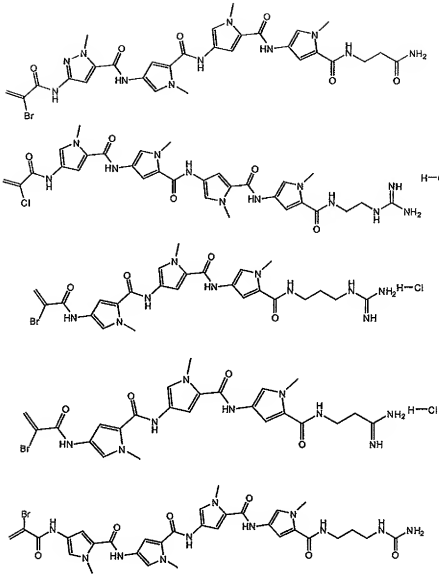












In these species, the specification has exemplified

R_1 is a bromine or chlorine atom;

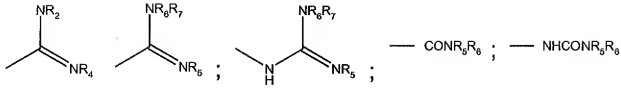
m is 0 or 1;

n is 3 or 4;

r is 0;

X and Y are, the same or different and independently for each heterocyclic ring, a nitrogen atom or a CH group;

B is:



R_4, R_5, R_6 and R_7 are hydrogen.

Applicants have narrowed these claims by deleting definitions in the Markush group so that the claims are closer in structure to the exemplification in the application. Further, the case law has held that mention of representative compounds may provide an implicit description upon which to base generic claim language. See, In re Robins, 429 F2d 452, 166 USPQ 552, (CCPA 1970).

The claims have also been amended to recite the specific tumors. These are recited on page 10, lines 1-3 of the instant specification.

No new matter has been added to the instant specification.

In support of the first rejection under 35 U.S.C. §112, for lack of descriptive support, the Office Action alleges that the specification discloses only a limited number of species on pages 6 and 7, but that the claims encompass a potentially huge genus. It is to be noted that the structure of formula I as recited in claim 1 in the response dated September 9, 2009 is described on page 4, line 1 to page 5, line 14 of the instant specification. As stated in MPEP 2163, "in claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claim encompass. Accordingly, such a formula is normally adequate description of the claimed genus", quoting Regents of the University of California v. Ell Lilly, 119 F3d 1589, 1568 43 USPQ 2d 1398, 1406 (Fed. Cir. 1999), cert denied, 523 US 1089 (1998).

Thus, there was descriptive support for the claims as originally filed. Applicants did not need to narrow the claims to respond to this rejection.

Moreover, as amended, there is descriptive support for the claimed subject matter. The heterocyclic groups have been amended to recite the specific heteryocyclic groups listed in the examples. The other variables m, n, r and B have been narrowed to the specific B groups in the examples. Thus, there is no question that applicants had possession of the claimed compounds at the time of the filing of the application. Therefore, the first rejection is obviated; withdrawal thereof is respectfully requested.

In support of the second written description requirement rejection, the Office Action has alleged that the term heterocycles ring, as defined in G is too broad and is not adequately described in the specification. Since r is 0, the rejection has been rendered moot. Thus, this rejection is obviated; withdrawal thereof is respectfully requested.

Pursuant to the rejection of the claims under 35 U.S.C. §103, the Office Action cites Cozzi et al. in view of Cortes.

Specifically, the Office Action contends that Cozzi et al. disclose the acryloyl distamycin derivative of formula I and Cozzi et al. disclose that the acryloyl distamycin derivatives can be combined with an additional antitumor agent for treating cancer or for ameliorating the conditions of mammals, including humans, suffering from cancer. Further, the Office Action admits that Cozzi et al. do not teach a protein kinase inhibitor. However, the Office Action contends that Cortes et al., the secondary reference, teach that CGP 57148 (ST1571) is a novel agent that inhibits the tyrosine kinase activity of ABL, and that clinical results suggest a very potent anti-leukemia activity with minimal toxicity in patients with Interferon-resistant Ph-positive CML. Further, the Office Action contends that, generally, it is

prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose. Thus, the Office Action asserts that combining the acryloyl distamycin compounds of Cozzi et al. with the ST1571 of Cortes et al. would achieve the compositions and methods of the present invention since they are both taught to be useful for treating leukemia.

Neither Cozzi et al. nor Cortes et al. teach, disclose or suggest the synergistic effect claimed. As evidence of the synergistic effect, reference is made to the in vitro data in Exhibit 1 submitted on November 7, 2007. The study showed using representative protein kinase inhibitors and compound of formula I that there is a synergistic effect.

The Office Action acknowledges the data presented in Exhibit 1.

In connection with the *in vitro* biological data submitted to the Examiner as "Exhibit 1" in applicants' response dated November 7, 2007, which shows the synergistic effect (i.e. more than additive effect) of the presently claimed composition, it appears that the Office Action recognizes the synergistic effect of the presently claimed composition, but indicates that the claimed subject matter is not commensurate in scope with the showing.

But, the claims are commensurate in scope of the showing. The compounds of formula I and the protein kinase inhibitor, as recited in the claims encompass the compounds tested. The combinations are, respectively, the combination of brostallicin (an α-bromo- or α-chloro-acryloyl-distamycin derivative of formula (I)) with ST1571 (a protein kinase inhibitor) on K562 human CML cell lines; the combination of brostallicin with ZD1839 (a protein kinase inhibitor) on human lung cancer NCI-H322M human lung cancer cell line, and the combination of brostallicin with OSI-774 (a protein kinase inhibitor) on MDA-MB-468 human breast carcinoma cell line. The *in vitro* data shows that, on human tumor cells, brostallicin can be

combined effectively with each of the above-identified three protein kinase inhibitors to produce a synergistic effect (i.e. more than additive effect)." The protein kinase inhibitors are OSI-774 and ST-1571 which are in the showing. Further, the compounds of formula I are commensurate in scope. The rings in R_2 are aryl including heteroaromatic, and the structures containing X and Y are aromatic, as defined and B contains moieties of imino, or their equivalent carbonyl functionality. In view of the above remarks, applicants submit that the claims, as presently amended, are not obvious over the applied references because the applied references, either alone or in combination, do not teach or suggest that the presently claimed composition, product or method has an antitumoral effect more than the additive antitumoral effect of the acryloyl distamycin derivative and the protein kinase inhibitor, which is fully supported by the data presented in Exhibit 1 as submitted along with applicants' response to U.S. Patent & Trademark Office dated November 7, 2007.

In view of the above remarks, applicants submit that the rejection under 35 U.S.C. §103(a) has been obviated. As such, reconsideration and withdrawal of the instant rejection is respectfully requested.

In view of foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

Peter I. Bernstein
Registration No. 43,497

Scully, Scott, Murphy & Presser, P.C.
400 Garden City Plaza, Suite 300
Garden City, New York 11530
(516) 742-4343
MJC/PIB:dk